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APPLICATION NO	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO	CONFIRMATION NO
09/463,844	02/01/2000	ANGELA VERONICA FLANNERY	PM265461	6871

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PILLSBURY WINTHROP LLP
1600 TYSONS BOULEVARD
MCLEAN, VA 22102

EXAMINER
CHERNYSHEV, OLGA N

ART UNIT	PAPER NUMBER
1646	12

DATE MAILED: 12/04/2001

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/463,844	Applicant(s) FLANNERY ET AL.	
	Examiner Olga N. Chernyshev	Art Unit 1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *10-12,17 and 22* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *10-12,17 and 22* is/are rejected.

7)☒ Claim(s) *10,11, 17, 22* is/are objected to.

8)☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *01 February 2000* is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15)☒ Notice of References Cited (PTO-892)
16)☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17)☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
18)☐ Interview Summary (PTO-413) Paper No(s). _____ .
19)☐ Notice of Informal Patent Application (PTO-152)
20)☐ Other: .

DETAILED ACTION

Election/Restrictions

1. Claim 17 has been amended, claim 22 has been added and claims 1-9, 13-16 and 18-21 have been cancelled as requested in the amendment of Paper No.10. Claims 10-12, 17 and 22 are pending.

2. Applicant's election of Group II, claims 10-12 and 17 in Paper No. 10 is acknowledged. Since Applicant did not present any arguments to traverse the restriction, response to restriction requirements is considered as election without traverse.

Claims 10-12, 17 and 22 are under examination in the instant office action.

Priority

3. Acknowledgment is made of applicant's claim for foreign priority. It is noted, however, that applicant has not filed a certified copy of the foreign priority document as required by 35 U.S.C. 119(b).

Drawings

4. The drawings filed on 02/01/2000 are acceptable subject to correction of the informalities indicated on the attached "Notice of Draftperson's Patent Drawing Review," PTO-948. In order to avoid abandonment of this application, correction is required.

5. The Figure 5 of the instant application is presented on separate pages or in separate panels. 37 C.F.R. § 1.84(u) (1) states that when partial views of a drawing which are intended to

form one complete view, whether contained on one or several sheets, must be identified by the same number followed by a capital letter. For example, the ten pages of Figure 5 in the instant specification should be renumbered "Figure 5A" – "Figure 5J" rather than "Figure 5". Applicant is reminded that once the drawings are changed to meet the separate numbering requirement of 37 C.F.R. § 1.84(u) (1), the specification should be amended to change the Brief Description of the Drawings and the rest of the specification to refer to each Figure accordingly. If, for example, Figure 5 is divided into Figures 5A-5J, then the Brief Description and all the references to this figure in the specification must refer to this Figure in the same manner.

6. It is noted that some figures of the instant application are not in compliance with the rules of sequences presented in drawing figures (see MPEP 2422.02). Appropriate correction is required.

Specification

6. The disclosure is objected to because of the following informalities: Pages 8-9 include list of references cited. It is suggested that references be included in the text of the specification. If Applicant adopts this suggestion a substitute specification will be required.

7. On page 3, lines 16-17 of the instant specification SEQ ID NO:1 is identified as "the ZGGBP1 gene having the full length cDNA", while on pages 11, line 23 SEQ ID NO:1 relates to "the translated amino acid sequence" and on page 12, line28 "The full length sequence of ZGGBP1 [a protein] [is] shown in SEQ ID NO:1". Clarification and appropriate correction are required.

Claim Objections

8. Claims 10 and 11 are objected to because of the following informalities: Sequence identifiers are not in compliance with the rules for presenting sequences in patent applications. See MPEP 2422.03. Appropriate format to present sequence is SEQ ID NO:2, for example. Appropriate correction is required.

9. Claims 17 and 22 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Applicant should note the "Infringement Test" for dependent claims in MPEP § 608.01(n). The test for a proper dependent claim is whether the dependent claim includes every limitation of the parent claim. A proper dependent claim shall not conceivably be infringed by anything, which would not also infringe the basic claim. In the instant case, the diagnostic assay claims could be infringed without infringing the claims from which it depends, i.e. the polypeptide claims. Therefore, they are improperly dependent and should be rewritten in independent form.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

10. Claims 10-12 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

The claims fail to include any limitations, which would distinguish the claimed proteins, peptides and compositions from those which occur in nature. In the absence of the hand of man, naturally occurring nucleic acid molecules and proteins are considered non-statutory subject matter. Diamond v. Chakrabarty, 206 USPQ 193 (1980). Additionally, mere purity of a naturally occurring product does not necessarily impart patentability. Ex parte Siddiqui, 156 USPQ 426 (1966). However, when purity results in a new utility, patentability is considered. Merck Co. v. Chase Chemical Co., 273 F. Supp. 68 (1967). Filing of evidence of a new utility imparted by the increased purity of the claimed invention and amendment of the claims to recite a purity limitation, if supported by the specification, is suggested to obviate this rejection. Applicant should point to the basis in the specification for any amendment to the claims.

11. Claims 10-12, 17 and 22 are rejected under 35 U.S.C. 101 because the claimed invention is drawn to an invention with no apparent or disclosed specific and substantial credible utility. The instant application has provided a description of an isolated DNA encoding a protein and the protein encoded thereby. The instant application does not disclose the biological role of this protein or its significance.

It is clear from the instant application that the polypeptides described therein are what is termed an "orphan proteins" in the art. The DNAs of the instant application have been isolated because of its similarity to a known DNAs. There is little doubt that, after complete characterization, these polypeptides may be found to have a specific and substantial credible utility. This further characterization, however, is part of the act of invention and until it has been

undertaken. Applicant's claimed invention is incomplete. The instant situation is directly analogous to that which was addressed in *Brenner v. Manson*, 148 U.S.P.Q. 689 (Sus. Ct. 1966), in which a novel compound which was structurally analogous to other compounds which were known to possess anti-cancer activity was alleged to be potentially useful as an anti-tumor agent in the absence of evidence supporting this utility. The court expressed the opinion that all chemical compounds are "useful" as it appears in 35 U.S.C. § 101, which requires that an invention must have either an immediate obvious or fully disclosed "real world" utility. The court held that:

> "The basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility", "[u]nless and until a process is refined and developed to this point-where specific benefit exists in currently available form-there is insufficient justification for permitting an applicant to engross what may prove to be a broad field", and "a patent is not a hunting license", "[i]t is not a reward for the search, but compensation for its successful conclusion".

The instant claims are drawn to polypeptides of as yet undetermined function or biological significance. It is clear from the instant application that the proteins described thereby and named ZGGBP1 of SEQ ID NO:2 and SEQ ID NO:4 are "homologous" to ned-4 human gene product and mouse nedd-4 gene product respectively. It has been stated in the instant specification that "The present invention is based on our discovery of a novel gene which maps to 18q21 and which unexpectedly shows appreciable sequence homology to the ned-4 gene on chromosome 15. Ned-4 is a human homologue of the mouse nedd-4 gene which is known to be differentially expressed during neural development and to be involved in signal transduction" (page 1, lines 28-32 of the instant specification). Further, the specification asserts that human

ned-4 and ZGGBP1 "have a high level of homology over much of the C-terminal region, including Hect and WW domains []. The presence of the se domains in ZGGBP1 suggests some common functionality with ned-4" (page 12, lines 6-10, emphasis added by the Examiner). Based on the homology of the claimed polypeptides to the known proteins, it was suggested that ZGGP1 would play similar roles in signal transduction, regulation of ion channels and other functions described for ned-4 and nedd-4 gene products. However, in the absence of knowledge of the biological significance of these specific polypeptides of SEQ ID NO:2 and 4 there is no immediately obvious patentable use for the claimed proteins. The instant specification provides a general description of affective disorders, bipolar disorder among them, without describing the relationship between the claimed polypeptides and the disorders. It is unknown and undisclosed in the instant specification what role the claimed polypeptides might play in the predisposition to, etiology or development of the "affective disorders". The similarity of the disclosed polypeptides potentially associated with "the affective disorders" does not make the instant polypeptides diagnostic of these disorders, or bipolar affective disorder type 1, in particular. There is no evidence of record, which associates the instant polypeptides with any diseases or disorder. To employ the claimed polypeptides in the future assays for measuring the presence or absence of ZGGBP1 proteins or in diagnostic assays for the detection of the protein is not a real world because it would eventually relate to a protein for which no biological function is known. The instant application also fails to demonstrate use of the proteins as markers for any disease or condition (which would be a real world use). Because the instant specification does not teach a biological activity of the claimed polypeptides, one cannot prevent or treat a condition or disease as implied by the specification. To employ the polypeptides of the instant invention in any of the

claimed assays would clearly be using it as the object of further research, which has been determined by the courts to be a utility, which, alone, does not support patentability. Since the instant specification does not disclose a credible "real world" use for the encoded protein then the claimed invention is incomplete and, therefore, does not meet the requirements of 35 U.S.C. § 101 as being useful.

12. Claims 10-12, 17 and 22 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a clear asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

13. Claims 10-12, 17 and 22 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claims 10-12, 17 and 22 are directed to polypeptides of SEQ ID NO:2 and 4 and homologues of polypeptides of SEQ ID NO:2 and 4. However, the instant specification fails to describe proteins, which are encompassed by these claims. In making a determination of whether the application complies with the written description requirement of 35 U.S.C. 112, first

paragraph, it is necessary to understand what Applicant has possession of and what Applicant is claiming. From the specification, it is clear that Applicant has possession of amino acid molecules of sequence of SEQ ID NO:2 and 4. The subject matter, which is claimed, is described above. First, a determination of the level of predictability in the art must be made in that whether the level of skill in the art leads to a predictability of structure; and/or whether teachings in the application or prior art lead to a predictability of structure. The claims are proteins homologous to the polypeptides of SEQ ID NO:2 and 4. First, the claims are not limited to the proteins with a specific amino acid sequence. The claims only require the polypeptide share some degree of structural similarity, or be homologous to the isolated proteins of SEQ ID NO:2 and 4. The specification only describes a polypeptides having the amino acid sequence of SEQ ID NO:2 and 4 and fails to teach or describe any other protein which lacks the amino acid sequence of SEQ ID NO:2 or 4 and is homologous to the polypeptides of SEQ ID NO:2 or 4. Therefore, there is a lack of guidance or teaching regarding structure and function because there is only a single example provided in the specification and because there is no guidance found in the prior art.

Next in making a determination of whether the application complies with the written description requirement of 35 U.S.C. 112, first paragraph, each claimed species and genus must be evaluated to determine whether there is sufficient written description to inform a skilled artisan that applicant was in possession of the claimed invention at the time the application was filed. With this regard, the instant application fails to provide a written description of the species or the genus which are encompassed by the instant claims except for the polypeptides of SEQ ID NO:2 and SEQ ID NO:4. The specification does not provide a complete structure of those polypeptides that are homologous to the polypeptides of SEQ ID NO:2 or 4.. The claims also

fail to recite other relevant identifying characteristics (physical and/or chemical and/or functional characteristics coupled with a known or disclosed correlation between function and structure) sufficient to describe the claimed invention in such full, clear, concise and exact terms that a skilled artisan would recognize applicant was in possession of the claimed invention. The specification fails to provide a representative number of species for the claimed genus (those proteins which are homologous to the polypeptides of SEQ ID NO:2 or SEQ ID NO:4) because the specification teaches only the two embodiments of SEQ ID NO:2 and 4. Therefore, the claims are directed subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

14. Claims 10-12, 17 and 22 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

15. Claims 10-11 are indefinite for the recitation of "homologues" of the polypeptides of SEQ ID NO:2 and 4. The metes and bounds of a "homologue" cannot be defined from the claims.

16. Claims 17 and 22 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The claims are directed to an assay without indicating any method steps.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

17. Claim 10 is rejected under 35 U.S.C. 102(b) as being anticipated by Hillier et al. (Genbank Accession No. N53633, 15 Feb 1996). Hillier et al. teach human NED4, a protein, which is "homologous" to and comprises a "fragment" of the claimed ZGGBP1 of SEQ ID NO:2 of claim 10.

18. Claim 11 is rejected under 35 U.S.C. 102(b) as being anticipated by Marra et al. (Genbank Accession No. W51213, 29 May 1996). Marra et al. teach mouse NED4, a protein, which is "homologous" to and comprises a "fragment" of the claimed ZGGBP1 of SEQ ID NO:4 of claim 11.

19. Applicant is advised that recitation of "fragments thereof" encompasses any protein with two amino acids in common with the disclosed proteins, as no size limitation on the "fragment" is indicated.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

20. Claim 12 is rejected under 35 U.S.C. 103(a) as being unpatentable over Karin et al. (US Patent 5,534,426, July, 1996).

Claim 12 is directed to a protein of claim 10 or claim 11 fused with glutathione-S-transferase (GST). Claims 10 and 11 are directed to polypeptides of SEQ ID NO: 2 and 4 and homologues and fragments thereof. As it was explained earlier in the instant office action, homologues and fragments of polypeptides of SEQ ID NO:2 and 4 are described and known in the art. Method of fusion of GST with a known protein for purification purposes, for example, in one-step glutathione-agarose chromatography, is also well known in the art. Therefore, it would be obvious for one skilled in the art to fuse the known in the art proteins with GST, using Karin et al. teachings as an example reference. One skilled in the art would be motivated to do so in order to subject the known proteins (homologues and fragments of SEQ ID NO:2 and 4) to a purification process.

Conclusion

21. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Olga N. Chernyshev whose telephone number is (703) 305-1003. The examiner can normally be reached on Monday to Friday 9 AM to 5 PM ET.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached on (703) 308-6564. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-0294 for regular communications and (703) 308-0294 for After Final communications.

Certain papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax center located in Crystal Mall 1 (CM1). The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)0. NOTE: If Applicant *does* submit a paper by fax, the original signed copy should be retained by Applicant or Applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers.

Official papers filed by fax should be directed to (703) 308-4556 or (703) 308-4242. If either of these numbers is out of service, please call the Group receptionist for an alternative number. Faxed draft or informal communications with the examiner should be directed to (703) 308-0294. Official papers should NOT be faxed to (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Olga N. Chernyshev, Ph.D. OC
November 30, 2001

CHRISTINE J. SAOUD
PRIMARY EXAMINER

Christine J. Saoud